[XX] the Sequence Listing in computer readable form, complying with §1.821(e) and §1.824, including, if an amendment to the paper copy is submitted, all previously submitted data with the amendment incorporated therein;

[ ] a substitute computer readable form to replace one found to be damaged or unreadable.

[ ] The computer readable form in this application no. 09/... is identical with that filed on .... [date sequence was filed] in application no. 09/ , filed [filing date]. In accordance with 37 C.F.R. §1.821(e), please use the [first-filed, last-filed or only, whichever is applicable] computer readable form filed in that application as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make the necessary change in application number and filing date for the instant application. A paper copy of the Sequence Listing is [included in the originally-filed specification of the instant application, included in a separately filed preliminary amendment for incorporation into the specification, whichever is applicable].

2. The description is believed to be in compliance with §1.821(d).

3. The undersigned attorney or agent hereby states as follows:

(a) this submission does not include new matter [§1.821(g)];

(b) the contents of the paper copy (as amended, if

applicable) and the computer readable form of the Sequence Listing, are the same [§1.821(f) and §1.825(b)];

(c) if the paper copy has been amended, the amendment is supported by the specification and does not include new matter [§1.825(a)]; and

(d) if the computer readable form submitted herewith is a substitute for a form found upon receipt by the PTO to be damaged or unreadable, that the substitute data is identical to that originally filed [§1.825(d)].

4. The Notice to Comply requires the payment of additional claims fees of $100 for two excess total claims, large entity. However, we previously deferred the application size fee, which is now paid herewith. If the AS2 fee was previously charged, prematurely, to our deposit account, then that charge should be reversed.

<table>
<tr><th colspan="4">APPLICATION AS FILED</th><th>FEE</th></tr>
<tr><td colspan="4">[ ] Basic Fee</td><td>paid</td></tr>
<tr><td colspan="4">[ ] Search Fee</td><td>paid</td></tr>
<tr><td colspan="4">[ ] Examination Fee</td><td>paid</td></tr>
<tr><td colspan="4">[X] Additional Fees for specification and drawings filed over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is $250 for each additional 50 sheets of paper or fraction thereof.</td><td></td></tr>
<tr><td>Total Sheets</td><td>Extra Sheets</td><td>No. of each additional 50 or fraction thereof (round up to a whole number)</td><td>Rate</td><td></td></tr>
<tr><td>173 -100</td><td>73/50</td><td>2</td><td>X$250.00</td><td>$500.00</td></tr>
<tr><td colspan="4">[X] Additional Claim Fees</td><td></td></tr>
</table>

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
TOTAL CLAIMS	22 - 20	2	X 50	$100.00
INDEPENDENT CLAIMS	1 - 3	0	X 200	
[ ] Multiple Dependent Claim First Presented			+360	
NON-SMALL ENTITY TOTAL				
[ ] Reduction of 1/2 for Small Entity				
TOTAL FILING FEE				$600.00

The PTO did not receive the following listed item(s) $600.00 credit Carol Foltz Reynolds

Credit Card Payment Form, PTO-2038, authorizing payment in the amount of $600.00 is attached.

The Commissioner is hereby authorized and requested to charge any additional fees which may be required in connection with this application or credit any overpayment to Deposit Account No. 02-4035. This authorization and request is not limited to payment of all fees associated with this communication, including any Extension of time fee, not covered by check or specific authorization, but is also intended to include all fees for the presentation of extra claims under 37 CFR Section 1.16 and all patent processing fees under 37 CFR Section 1.17 throughout the prosecution of the case. This blanket authorization does not include patent issue or publication fees under 37 CFR Section 1.18.

The PTO did not receive the following listed item(s)

5. Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of "Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of the sequence under <213>.

Hence, counsel may choose to identify a listed sequence

as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

The Examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the results of his or her sequence search against a database containing known natural sequences.

6. The Notice to Comply says that "Annexes have not been entered because Not a pafe [sic] for page substitution (pg. 20)". We believe this is a reference to the March 3, 2005 response to written opinion, which enclosed substitute page 20. We agree that substitute page 20 appears to be lacking the first line of the original page. However, we submit that it constitutes an instruction to enter the "TM" at the five

locations indicated. We enclose a mark up of the original page 20, marked-up as intended by the March 3, 2005 response and ask that it be substituted.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By: _____
Iver P. Cooper
Registration No. 28,005

Enclosures
-CRF
-Sequence Listing
-Copy of Notification to Comply...
-Mark-up page 20

IPC:lms
624 Ninth Street, N.W.
Washington, D.C. 20001
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\ipc\g-i\hoib\ST. HILAIRE1A\pto resp seqlist.wpd

French Press and sonicator. The extraction procedure can be manipulated to enrich for low abundance proteins or to isolate a particular class of proteins. General protocols for the extraction of proteins from different organisms are readily available. See, for example, *2-D Proteome Analysis Protocols*, A.J. Link (Ed), 1st Ed, 1999, Humana Press: Totowa)

Detecting

A variety of suitable methods are useful for detecting the ligand-protein binding pairs. For example, where a single protein mixture is used (see Figure 1), the extracted protein may be immediately incubated with the immobilized ligand library, and, after washing, bound protein can be detected directly in the binding complex by the application of a detection molecule to the incubation mixture, such as silver or fluorescent dye that does not interact with the ligand or the solid support. It is however generally preferred that the protein mixture is labeled with a detection probe prior to incubation with the ligand library. Hence, in another embodiment, the mixture of proteins may be labeled with a detection probe, for example, with a fluorescent dye such as Oregon Green 514™ (green; See Example 11), N-mehtyl anthranilate (blue; See Example 13), Rhodamine red™ (red; See Example 11), cyanine dye 2™, cyanine dye 3™, cyanine dye 5™ or other commonly used fluorescent probes. See for example, Richard P. Haugland, "Handbook of Fluorescent Probes and Research Products", 9th Edition, 2002, Molecular Probes Europe BV: Leiden or world wide web (WWW) sites "probes.com" and "amershambio-sciences.com/aptrix/upp00919.nsf/Content/DrugScr+CyDye+Fluors+introduction" for a description of cyanine fluorescent dyes. The detection probe may also be a fluorescent protein, such as Green fluorescent proteins or fluorescent mutants thereof. The detection probe can also be a probe that produces chemoluminescence, such as luciferase or aequorin. In these embodiments, after incubation of ligands with proteins, the library is washed and ligand-protein binding complexes will be detected via the label, for example, fluorescence or color. These ligand-protein binding pairs can be immediately isolated using automatic or manual sorting procedures. If the detection probe is a fluorescent probe, then automatic sorting preferably involves the use of a FABS and/or a fluorescence activated beads sorter. The detection probe may furthermore be a compound capable of producing chemiluminescence, such as for example luciferase or aequorin. The detection probe may furthermore be an enzyme capable of catalyzing a detectable reaction, such as for example phosphatase or peroxidase. The detection probe may furthermore be a metal, for example gold. The protein mixture may be labeled with the detection probe by any conventional method depending on the nature of the detection probe.